REMARKS

Claims 3-5 and 39 are pending in the present application. Claims 1-2 and 6-38 have been canceled. Claims 3 and 39 have been amended herein and claims 40-42 have been added.

The Office has indicated that the inventor's declaration is defective. Applicants submit herewith a new declaration in compliance with 37 C.F.R. §1.67(a) appropriately claiming benefit of earlier filed U.S. and PCT applications. Applicants respectfully request that any objection to the inventors' declaration be withdrawn.

Claims 3-5 and 39 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. More specifically, the Office rejected claim 3 because it was said to be unclear in the preamble what the etiological agents are due to the insertion of the "distinct" limitation. Claim 3 has been amended to delete the reference to 12-HETE. Applicants submit that this amendment obviates the rejection and respectfully request that this rejection be withdrawn. New claim 40 includes the "distinct" limitation mentioned in the Office Action in a wherein clause. Applicants submit that this claim complies with 35 U.S.C. §112.

Claim 4 was rejected because the Office stated the Markush group is unclear because it is not clear if a comma is intended between "condition" and atherosclerosis. This claim has been amended for clarity. Applicants submit that the claim fully complies with the standards for clarity and respectfully request that the Office withdraw this rejection.

Finally, the Office rejected claim 39, stating that the phrase "said tissue specimen" lacks antecedent basis. Claim 39 has been amended to avoid use of this term. Applicants therefore request that this rejection be withdrawn.

Claim 39 was rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification as to reasonably convey to one skilled in the art that the inventor, at the time of the application was filed, had possession of the invention. Specifically, the Office Action expresses the opinion that claim 39 recites a Markush group member ("endothelial cells") but disclosed only "aortic endothelial cells" and "arterial endothelial cells." Applicants have amended claim 39 to recite "aortic" and "arterial" endothelial cells. Applicants therefore request that the rejection be withdrawn.

Claims 3-5 and 39 were rejected under 35 U.S.C. §112, first paragraph, on grounds of non-enablement, stating that the claimed method of diagnosis is incomplete because there is no final step that relates the presence of the determined etiological agent to the presence of the disease state in the patient. Applicants have amended claim 3 to include a final step within the claim. Therefore, Applicants request that the rejection under 35 U.S.C. §112, first paragraph, be withdrawn.

Claims 3-5 and 39 were rejected under 35 U.S.C. §112, first paragraph, on the grounds that the specification does not reasonably provide enablement for the diagnosis of a disease state by the detection of antibodies to 12-LO to 12-HETE. Claim 3 has been amended to delete references to antibodies. Therefore, Applicants request that the rejection based on an asserted lack of enablement under 35 U.S.C. §112, first paragraph, be withdrawn.

Claims 3-5 were rejected under 35 U.S.C. §102(b) and under 35 U.S.C. §103(a) as being unpatentable over Jost-Vu *et al.* (hereinafter "Jost-Vu"). The Office reasons that Jost-Vu discloses a measurement of elevated levels of 12-HETE in human patients with NIDDM. Thus, the Office argues that claims 3-5 are anticipated and obvious.

To anticipate under §102, a reference must disclose each and every element of the claimed invention. See M.P.E.P. §2131. Jost-Vu teaches that diabetics have an increase in HETE. Claim 3 has been amended to avoid this term. Thus, Applicants submit that Jost-Vu does not teach each and every limitation of the invention claimed in claims 3-5. Therefore, the amendment obviates the rejection under 35 U.S.C. §102(b). Applicants request that the rejection be withdrawn.

To make out a *prima facie* case of obviousness against a claim, the Office must meet three criteria: (1) the cited prior art reference must teach or suggest each and every element of the rejected claim, (2) there must be motivation to combine or modify what is fairly disclosed in the reference to achieve the claimed invention and (3) there must be a reasonable expectation of success. M.P.E.P. §2143. Applicants respectfully submit that the Office cannot make out a *prima facie* case of obviousness with respect to the presently claimed invention based on the Jost-Vu reference.

As a first matter, the reference does not teach or suggest each and every element of the amended claims for the reasons discussed above with respect to anticipation. For this reason alone, the case for obviousness fails. Jost-Vu does not disclose a method for diagnosing a disease state in which 12-LO is the etiological agent. Rather, Jost-Vu discloses or suggests only that an increase in 12-HETE may play a role in diabetic vascular disease. A method as recited in claim 3 is not disclosed or suggested.

Moreover, there is no suggestion or motivation to modify the prior art teaching of Jost-Vu to obtain the claimed invention. An increase in HETE playing a role in diabetic vascular disease does not provide any suggestion or motivation to modify the prior art teaching to search for a particular 12-LO protein and

determine its level. Therefore, the Office cannot meet the second criterion necessary to make out a *prima facie* case of obviousness.

Finally, there is no reasonable expectation of success of achieving the invention claimed here. Even if the skilled person were to happen on a particular lipoxygenase enzyme, a successful diagnostic method would not be reasonably expected because, as the Office points out, "any 12-LO, no matter what its cellular source, produces 12 HETE ...." Thus, it could not be known which, if any, of the known LO enzymes could have been responsible. Therefore, the skilled person could not have expected that a particular 12-LO would serve as a successful diagnostic indicator.

In summary, the Office cannot meet even one of the necessary criteria to make out a *prima facie* case of obviousness of the amended claims. Applicants respectfully submit that the rejection based on obviousness under 35 U.S.C. §103 (a) over the Jost-Vu reference should be withdrawn.

The Office Action refers to claim 39 as obvious and states on page 6 that the teaching in Jost-Vu concerning the role the LO pathway may play in diabetic vascular disease would have "led one to consider vascular smooth muscle or vascular endothelial samples" (emphasis added). Applicants respectfully submit that this is not the standard for obviousness under 35 U.S.C. §103. The Office has used an impermissible "obvious-to-try" standard, without showing any reasonable expectation of success. See M.P.E.P. § 2143.02; In re O'Farrell, 853 F.2d 894, 7 U.S.P.Q.2d 1673 (Fed. Cir. 1988). Applicants submit that any rejection of claim 39 based only on the reasoning that Jost-Vu would have "led one to consider" a course of action is not proper and should be withdrawn. The reference does not teach or suggest every element of claim 39, does not provide motivation to modify its teachings

and fair suggestions and does not provide even the slightest expectation of success, much less a reasonable expectation.

For the above reasons, Applicants request favorable consideration and allowance of the claims.

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